REMARKS

Applicants herewith submit amendments to the specification to correct editorial errors that were heretofore unnoticed and to incorporate SEQ ID NOS. A Sequence Listing is also herewith submitted.

Claims 246-270 are pending in the above-referenced application. Claims 261 and 263 have been cancelled. Claims 246, 247, 248, 257, 258, 261, 262, 264, 265, 267 and 268 have been amended to more distinctly claim that which Applicants regard as their invention and to advance prosecution. No new matter has been added. The claim amendments are supported by the specification.

Applicants additional request consideration of the Information Disclosure Statement submitted on October 27, 2003. A copy of said Information Disclosure Statement is attached hereto.

The Rejection Under 35 U.S.C. 112, First Paragraph-Written Description

Claims 246-270 have been rejected under 35 U.S.C. 112, first paragraph as lacking an adequate written description. Applicants asserted in the response filed 2/28/02 that an adequate description has been provided and point to pages 33-47 and 53 of the specification to teach descriptions of the claimed constructs. Applicants' further pointed to figures 1-7 to show use of drawings to show description of the claimed invention. Applicants' further noted that actual reduction to practice is not required to satisfy the written description requirement.

The Examiner responded by stating that MPEP 2163 teaches the following conditions for the analysis of the claimed invention at the time the invention was made in view of the teachings of the specification and level of skill in the art:

> The claimed invention as a whole may not be adequately described when an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-

> recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence...A lack of written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process...Generally, there is an inverse correlation between the level of skill and knowledge in the art and the specificity of disclosure necessary to satisfy the written description requirement...The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structures or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

Applicants respectfully traverse the rejection. First, Applicants note that claim 246 has been amended to be directed to a chemically modified nucleic acid construct which produces a nucleic acid product having biological activity when present in a cell; the nucleic acid product is a modified nucleotide, a nucleotide analog, a non-nucleic acid entity, and a combination of the foregoing, and said product being selected from the group consisting of antisense RNA, antisense DNA, sense RNA, ribozymes, decoys, messenger RNA, protein or a combination of any of the foregoing. An adequate written description is provided of the

subject matter recited in amended claim 246 and the other pending claims. As will be discussed in further detail below, a very detailed description of the constructs of the present invention is provided in the specification on pages 34-47 and in Examples 1-7.

Additionally, in the Office Action, the Examiner stated that the specification as filed teaches in the figures numerous potential constructs using certain modified features for production of products in a cell. Primarily, the specification teaches vector-like constructs having features which are meant to enhance the vector-like constructs for targeting the expressed product in a cell. Such vector-type constructs require specific sequences of nucleic acids, modified nucleotides or analogs for the expression of the claimed products: antisense RNA, antisense DNA, sense RNA, ribozymes, decoys, messenger RNA or protein.

The Examiner further stated that

> Neither the specification nor the drawings provided a clear picture of the completed vector-type constructs contemplated, such that one of skill in the art would have been able to immediately envisage the finished product since a representative number of species of such constructs is not adequately described by the most basic necessary chemical and physical structure of nucleic acid constructs, the nucleic acid sequence structure. Most of the drawings in the instant specification taught "ball and stick" vector-type constructs having a partial idea of the pertinent features of the vectors, but not having a substantially complete sequence. Applicant argues that a reduction to practice is not necessary at the time of the invention, but in the instant case, knowledge of the sequence would be necessary for synthesizing the actual constructs. When considering that instant claim 246 claims any vector construct made of nucleic acids that when present in a cell produces a product, the breath of the claimed invention is extremely

> broad. From viewing the drawings, for instance figures 1-7 as pointed out by Applicant, one of skill in the art would envision a primer with any ligand(s) attaching to what appears to stand for a nucleic acid vector and primers having fusogenic peptides and tails. The specification teaches prophetically on pages 33—47 the design of any vector construct having such ligands and additional modifications. There is no evidence on the record of a relationship between the structures of the lines and features in drawings 1–7 for instance to specific nucleic acid sequences of vectors or the use of known vectors from which specific modifications may be added. Sequence structure of nucleic acids is a necessary stating point for making a vector for expression of nucleic acid products as claimed. One of skill in the art would have not recognized that Applicant was in possession of a representative number of species of any finished expression vectors in view of the teachings of figures 1-7 and pages 33-47 of the specification since no specific guidance was given for the design of the most basic elements of the claimed nucleic acid constructs. The scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural difference between genus members I permitted. Although the specifications states that these types of changes are routinely done in the art, the specification and claim do not provide any guidance as to what changes should be made and in what order. The general knowledge and level of skill in the art do not supplement the omitted description of sequence structure, as starting point for instance, because specific, not general, guidance is what is needed for making the finished constructs. For these reasons, Applicant was not in possession of the claimed genus at the time the invention was made.

Applicants respectfully traverse rejection. While the Examiner notes that Figures 1 to 7 lack any sequence information and that this is a necessary

element for the teaching of the present invention, Applicants respectfully submit that such sequences are not necessary. In Applicants' view, for any given construct that is synthesized according to the direction of the present invention, the sequence construct, will be important to the practitioner, but specific sequences are not needed for an understanding of how the invention is generally practiced.

A knowledge of the specific sequences that the applicants would have used in the examples of the application would not provide any useful additional teaching elements which a practitioner would need in practicing the present invention using their particular constructs. Moreover, the use of graphics that employ lines demarcating functional elements such as ligands and fusogenic proteins and complementarity between nucleic acid strands should be sufficient in that the particular sequences represented by such lines are not required to understand the relationships that are being depicted. The MPEP in section §2163 II.A.3. (a) states:

> An applicant may show possession of an invention by disclosure of drawings or structural chemical formulas that are sufficiently detailed to show that applicant was in possession of the claimed invention as a whole..... The description need only describe in detail that which is new or not conventional..... This is equally true whether the claimed invention is directed to a product or a process.

The stick figures presented in the figures were certainly standard for figures presented by those of ordinary skill of the art to describe a construct or composition. Furthermore, examples have been given that would generate constructs depicted by these figures.

For instance, Example 1 provides an example of starting with a single-stranded circle with an F1 packaging signal. At the time of the submission of the

application, there were numerous vectors available with complete information available concerning their sequences and genetic characteristics. A skilled practitioner of the art would have been able to use such cloning vectors to insert nucleic acid sequences coding for biological functions that would have been of interest to the practitioner (such as antisense, mRNA or decoys). Such cloning procedures were an ordinary practice of the art at the time of the filing of the application. Further in the example, the synthesis of a primer is described. As mentioned above, the sequences of the cloning vectors are known and additionally, due to the orientation of the F1 packaging signal, the particular strand that would be produced after infection by a helper phage would also be known. As such, it would be a simple matter for a skilled practitioner of the art to decide which particular sequences of his construct should be used to design the allyl amine-modified oligonucleotide described in the example. Further, in the example, methods are disclosed for the preparation of a ligand and its attachment to an allyl-amine oligonucleotide. This was a general method that could be used for any nucleic acid that comprised allyl amine moieties. Hybridization of this oligonucleotide would result in a nucleic acid construct depicted in Figure 1a.

Example 2 described the use of the product of Example 1 in a strand extension reaction to produce a double stranded DNA molecule shown in Figure 1B.

Example 3 describes the preparation of a two segment chemically modified nucleic acid construct (CHENAC) in which one segment has dispersed ligands and chemical modifications and is depicted in Figure 2.

Example 4 describes the preparation of a two segment CHENAC in which one segment has dispersed ligands and chemical modifications incorporated by

ribonucleotides moieties and is depicted in Figure 3. The lower part of the diagram contains a brief description of its use.

Example 5 describes the preparation of a three segment CHENAC containing a modified single stranded tail and is depicted in Figure 4. An intermediate product is shown in Figure 5.

Example 6 describes the preparation of a three segment CHENAC containing an unmodified single stranded tail capable of hybridizing to homopolymers containing ligands. Its preparation is depicted in Figure 6.

Example 7 describes the construction of an RNA derived CHENAC and is shown in Figures 7 and 8. Furthermore, variations of example 7 are described in Examples 8-10 and depicted in Figures 9-10.

In general, there is an abundance of information on how a practitioner can apply the present invention to transforming their plasmid into the various constructs that have been disclosed in the invention. As such, there is no undue experimentation required for the practice of the present invention as a result of the information provided in the Description of the Invention, Figures and Examples.

To summarize, Applicants would like to stress that as described in Example 1, any plasmid, from a variety of commercial sources, containing an F1 packaging signal may be used. In view of the above arguments, Applicants would like to assert that the rejection under 35 U.S.C. § 112, first paragraph, has been overcome. Applicants therefore respectfully request that the rejection be withdrawn and that claims 246-270 are allowed.

The Rejection Under 35 U.S.C. 102(e)

Claims 246-270 have been rejected under 35 U.S.C. §102(e) as being anticipated by Meyer et al. The Examiner stated that Applicants asserted that

Meyer et al. does not teach constructs defined by the instant specification and stated that the ODN-peptide conjugates of Meyer et al. clearly are not construct because "the conjugates cannot integrate into cellular nucleic acid or exist in an extrachromosomal site. The ODN-peptide conjugates certainly cannot propagate copies of itself in either the integrated or extrachromosomal state. In other words, the ODN-peptide conjugates of Meyer et al. are not capable of self replication." The Examiner responded by stating that Applicants are arguing limitations of the claimed constructs which are not present in the claims. The claims do not require that the constructs integrate into cellular nucleic acid or exist in an extrachromosomal state, nor that they can propagate copies and are capable of self replication. Claim 247 recites wherein the construct is linear. The claims don't recite that such linear constructs self-replicate.

Applicants respectfully traverse the rejection. However, before addressing the rejection, Applicants note that Applicants have amended claim 246 to recite that the construct is a chemically modified nucleic acid construct ,which when present in a cell produces a nucleic acid having biological activity and comprises a modified nucleotide, a nucleotide analog, a non-nucleic acid entity, and a combination of the foregoing, and said product being selected from the group consisting of antisense RNA, antisense DNA, sense RNA, ribozymes, decoys, messenger RNA, and/or protein. Claim 268 has been amended to recite that the construct comprises at two or more location chemical modifications or ligands. The amendment was made to more distinctly claim the subject matter of the invention and to advance prosecution and is not in acquiescence to the Examiner's position. Applicants reserve the right to file subsequent continuation and/or divisional applications on cancelled subject matter.

Applicants assert that Meyer et al. does not teach the subject matter recited in independent claims 246 and 268. Specifically, the ODN-peptide

conjugate is not a construct. A "DNA construct" has been defined at http://www.kumc.edu/gec/gloss.html as "A DNA sequence that has been modified to yield a recombinant DNA molecule"

In contrast, the conjugate of Meyer et al. is merely an oligonucleotide attached to a polymer carrier via a peptide linker. The conjugate of Meyer is a conjugate **not** a construct. Additionally, amended claim 268 recites that the chemical modification or ligand is attached to the construct at two or more locations. Secondly, no nucleic acid product was actually synthesized by the conjugate of Meyer et al. Actually, Meyer et al. describes a procedure that induces only degradation of a messenger RNA target.

The dependent claims 247-253, 255-262, 264-267 would not be anticipated by Meyer et al. since they depend from claim 246. Claims 269-270 are also not anticipated by Meyer et al. since they depend from claim 268.

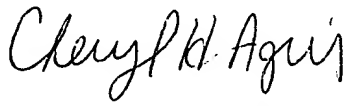
In view of amended claim 246 and 268, the pending claims are not anticipated by Meyer et al. Therefore, Applicants respectfully request that the rejection be withdrawn.

Summary and Conclusions

Claims 246-270 are presented for further examination. No further claims have been presented.

If a telephone conversation would further the prosecution of the present application, Applicants' undersigned attorney request that he be contacted at the number provided below.

Respectfully submitted,



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